Dermatology Practical & Conceptual

Efficacy and Safety of Ixekizumab Versus Adalimumab in Biologic-naïve Patients With Active Psoriatic Arthritis and Moderate-to-severe Psoriasis: 52-week Results From the Randomized SPIRIT-H2H Trial

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ABSTRACT

Introduction: The randomized, open-label, assessor-blinded, parallel-group SPIRIT-H2H trial (NCT03151551) demonstrated superiority of ixekizumab over adalimumab in simultaneously achieving improvement in joint symptoms (American College of Rheumatology [ACR]50) and skin clearance (Psoriasis Area and Severity Index [PASI]100) in biologic-naïve patients with active psoriatic arthritis (PsA) and plaque psoriasis (PsO) at Week (W) 24. Higher efficacy of ixekizumab versus adalimumab was maintained through W52.

Objectives: This analysis investigated efficacy and safety of ixekizumab and adalimumab in the subgroup of patients with PsA and moderate-to-severe PsO through W52.

Methods: Efficacy and safety outcomes were analyzed in patients with PsA and moderate-to-severe PsO (PASI ≥ 12, Body Surface Area ≥ 10%, static Physician Global Assessment ≥ 3) through W52. Categorical and continuous outcomes were analyzed using logistic regression models and mixed model for repeated measures, respectively.

Results: More ixekizumab- versus adalimumab-treated patients simultaneously achieved PASI100 and ACR50 at W24 (40.8% versus 17.6%, P = 0.015) and W52 (38.8% versus 17.6%, P = 0.026). Likewise, more ixekizumab- versus adalimumab-treated patients achieved PASI100 (59.2% versus 25.5%, P = 0.001) and PASI90 (81.6% versus 60.8%, P = 0.028) through W52, and nail PsO clearance at W24. Joint symptom improvements were comparable between groups. No new safety findings were reported.

Conclusions: Ixekizumab had higher efficacy than adalimumab in simultaneous achievement of ACR50 and PASI100 at W24 and W52 in patients with PsA and moderate-to-severe PsO. Ixekizumab-treated patients showed higher response rates for nail PsO clearance and for reporting minimal or no impact on quality of life at W24.

Introduction

Plaque psoriasis (PsO) is a chronic, inflammatory skin condition that has a high disease burden and significantly impacts patients' quality of life (QoL), especially in those with moderate-to-severe disease and involvement of difficult to treat areas, such as the nails. Psoriatic arthritis (PsA) is a chronic, immune-mediated, seronegative spondylarthritis associated with musculoskeletal and non-skeletal manifestations. A personal or familial history of PsO is one of the diagnostic criteria for PsA, as PsO commonly precedes the development of PsA [1]. Up to 30% of patients with PsO will develop PsA, in particular those with scalp, intergluteal/perianal and nail involvement, further increasing the disease burden and reducing QoL [1-4]. The prevalence of nail PsO, a painful and burdensome manifestation, is higher in PsA than PsO [5,6]. One possible explanation of this is the anatomical connection between the nail matrix and structures of the distal interphalangeal joint [7]. Therefore, successful treatment of both joint and skin symptoms is important in achieving optimal improvements to health-related QoL in patients with PsO and PsA, with clearance of co-existing nail PsO providing additional benefits [8]. First-line treatments for PsO and PsA include conventional systemic therapies and conventional systemic disease modifying anti-rheumatic drugs (csDMARDS), respectively. For patients with inadequate responses to these, the European Dermatology Forum and European League Against Rheumatism recommend the use of biologics targeting inflammatory cytokines, such as interleukin (IL)-17A and tumor necrosis factor (TNF) [9,10]. Biologics inhibiting either IL-17 or TNF (such as adalimumab [ADA]) signaling pathways have demonstrated high efficacy in improving joint symptoms in patients with PsA in randomized clinical trials [11–19]. As higher rates of skin clearance have been observed for anti-IL-17 versus anti-TNF biologics, the comparative efficacy of these biologics in patients with concurrent PsA and moderate-to-severe PsO should be investigated [15,18–22].

Objectives

Ixekizumab (IXE), a high-affinity monoclonal antibody that selectively targets IL-17A, is efficacious in patients with PsO and/or PsA [15,17,21,23]. The SPIRIT-H2H trial, the first direct comparison of IXE and ADA in biologic-naïve patients with active PsA and PsO, reported that significantly more IXE- versus ADA-treated patients simultaneously achieved American College of Rheumatology (ACR)50 and complete clearance of PsO at Week (W) 24 and W52 [18,19]. This analysis aims to compare the efficacy of IXE versus ADA through W52 in the subgroup of patients with active PsA and moderate-to-severe PsO in the SPIRIT-H2H trial, who received dosage regimens per approved label for moderate-to-severe PsO. As this subgroup is reflective of the patients eligible for biologic treatment in routine dermatological clinical practice, this analysis will inform treatment decisions in these settings.

Methods

Participants and Study Design

SPIRIT-H2H (Clinicaltrials.gov: NCT03151551) is a 52-week, multicenter, randomized, open-label, assessor-blinded, parallel-group study evaluating the efficacy and safety of IXE versus ADA in biologic-naïve, csDMARD-inadequate-responder patients with active PsA and PsO. The study population and study design have been previously published [18]. Briefly, patients were aged ≥ 18 years, had a confirmed diagnosis of PsA of ≥ 6 months, had active PsA (≥ 3/66 swollen joints and ≥ 3/68 tender joints) and PsO (≥ 3% of the Body Surface Area [BSA] affected), fulfilled the Classification for Psoriatic Arthritis (CASPAR) criteria and were not previously treated with biologics or Janus kinase inhibitors. Patients on csDMARDs at screening were permitted to continue at a stable dose. Randomization was stratified by concomitant csDMARD use and moderate-to-severe PsO involvement (PASI ≥ 12, BSA ≥ 10%, and static Physician Global Assessment [sPGA] ≥ 3) at baseline.

Patients were randomized at a 1:1 ratio to receive IXE or ADA. Patients with active PsA and moderate-to-severe PsO were treated as per approved label for moderate-to-severe PsO and received a 160 mg IXE starting dose at W0, followed by 80 mg IXE every 2 weeks (Q2W) from W2 to W12 and every 4 weeks thereafter, or an 80 mg ADA starting dose, followed by 40 mg ADA Q2W starting at W1.

In this post hoc analysis, only patients with active PsA and moderate-to-severe PsO at baseline were included.

SPIRIT-H2H was conducted in accordance with the ethical principles of the Declaration of Helsinki. The study protocol was approved by the ethical review boards of all participating sites prior to the start of study-related procedures. Informed consent was obtained from all participants.

Efficacy Endpoints

Endpoints were assessed in all patients with active PsA and moderate-to-severe PsO at baseline. The primary endpoint of SPIRIT-H2H was the proportion of patients who simultaneously achieved ACR50 and PASI100 responses at W24. Major secondary endpoints were the proportion of patients achieving ACR50 and the proportion of patients achieving PASI100 at W24.

Endpoints at W52 included the proportion of patients simultaneously achieving ACR50 and PASI100 responses, PASI100, PASI90 or PASI75 responses, change from baseline in Dermatology Life Quality Index (DLQI) total score, proportion of patients achieving DLQI (0,1), change from baseline in the Itch Numeric Rating Scale (NRS) score, proportion of patients achieving Itch NRS score = 0, and change from baseline in the Nail Psoriasis Severity Index (NAPSI) fingernails score and proportion of patients achieving complete clearance of nail psoriasis (NAPSI = 0) in the subgroup of patients with NAPSI ≥ 1 at baseline.

Safety

Treatment-emergent adverse events (TEAEs) were defined as events that initially occurred or worsened in severity after the first dose of the study treatment and on or before the date of the final visit within the treatment period. Adverse events (AEs) of special interest included infections, injection site reactions, malignancies, major adverse cardiovascular events, allergic reactions/hypersensitivity, inflammatory bowel disease, depression, hepatic laboratory changes, cytopenia, and neutropenia. Cerebrocardiovascular events were adjudicated by external clinical events committees. Safety results for the total study population have been published previously [18,19].

Statistical Analysis

Efficacy

In this post hoc analysis, efficacy analyses were performed on the intent-to-treat population, consisting of all randomized patients according to the treatment assigned at W0. Categorical variables were assessed using logistic regression models with treatment and concomitant csDMARD use at baseline as factors, as well as Fisher's exact tests whenever relevant. The non-responder imputation (NRI) method was used in case of missing data: patients were considered non-responders if they did not meet the clinical response criteria or had missing clinical response data at a particular time point of analysis. Continuous variables were analyzed using a mixed effects model of repeated measures analysis, which included treatment group, concomitant csDMARD use at baseline, and visit as fixed factors, baseline value as a covariate, and baseline-by-visit and treatment-by-visit interaction terms.

Safety

Descriptive statistics were performed on the safety population, defined as all randomized patients who received ≥ 1 dose of the study treatment.

Results

Baseline Characteristics

Of the 566 biologic-naïve patients included in the SPIRIT-H2H study, 49 (17.3%) of the IXE-treated patients and 51 (18.0%) of the ADA-treated patients had moderate-to-severe PsO (PASI ≥ 12, sPGA ≥ 3, and BSA ≥ 10%) at baseline. The frequency of moderate-to-severe PsO and nail PsO in the overall SPIRIT-H2H population is visually

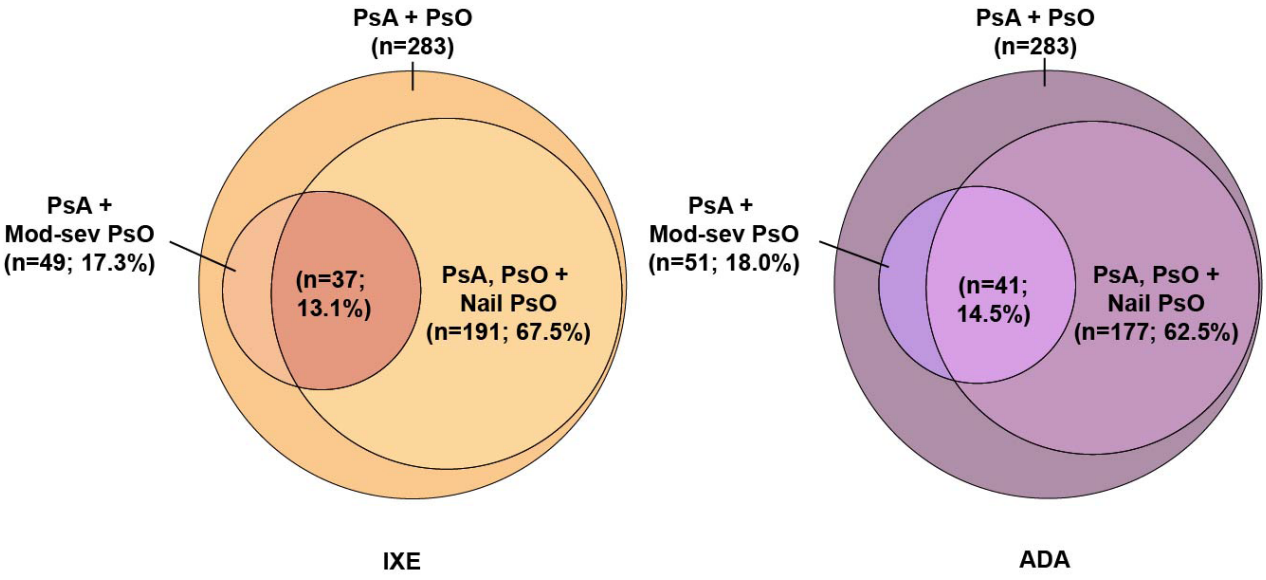

Figure 1. Schematic representation of moderate-to-severe psoriasis and nail psoriasis frequency in the SPIRIT-H2H patient population. Venn diagrams show the proportion of patients with moderate-to-severe PsO and nail PsO (NAPSI ≥ 1) in the IXE (n = 283) and ADA (n = 283) groups of the entire SPIRIT-H2H population at baseline.

ADA = Adalimumab; IXE = Ixekizumab; Mod-sev = Moderate-to-severe; NAPSI = Nail Psoriasis Severity Index; PsA = Psoriatic arthritis; PsO = Plaque psoriasis.

Table 1. Baseline demographics and disease characteristics of patients with PsA and moderate-to-severe PsO

Category	IXE (n = 49)	ADA (n = 51)
Age (years)	45.3 ± 11.5	46.3 ± 11.3
Male, n (%)	30 (61.2)	33 (64.7)
BMI (kg/m^2)	29.5 ± 7.3	30.2 ± 8.7
Duration of symptoms since PsO diagnosis (years)	17.0 ± 10.5	15.0 ± 11.3
Duration of symptoms since PsA diagnosis (years)	7.0 ± 7.4	5.7 ± 6.2
PASI	22.9 ± 10.5	20.5 ± 7.3
sPGA	3.6 ± 0.7	3.6 ± 0.7
Percentage BSA	41.2 ± 24.1	32.5 ± 19.3
Fingernail NAPSI ≥ 1, n (%)	37 (75.5)	41 (80.4)
Fingernail NAPSI	26.1 ± 21.6	23.3 ± 18.5
Fingernail NAPSI > 16, n (%)	21 (42.9)	24 (47.1)
Fingernail NAPSI > 40, n (%)	10 (20.4)	7 (13.7)
Itch NRS	6.5 ± 2.5	7.6 ± 1.8
DLQI	16.9 ± 7.3	16.7 ± 6.4
Tender joint count	24.2 ± 15.7	23.9 ± 15.5
Swollen joint count	12.4 ± 9.7	13.0 ± 11.0
CRP level (mg/L)	14.5 ± 21.7	17.6 ± 28.9
Concomitant MTX use, n (%)	25 (51.0)	28 (54.9)

Unless indicated otherwise, data are presented as mean ± SD.

ADA = Adalimumab; BMI = Body Mass Index; BSA = Body surface area; CRP = C reactive protein; DLQI = Dermatology Life Quality Index; MTX = Methotrexate; NAPSI = Nail Psoriasis Severity Index; NRS = Numeric Rating Scale; PASI = Psoriasis Area and Severity Index; PsA = Psoriatic arthritis; PsO = Plaque psoriasis; SD = Standard deviation; sPGA = Static Physician Global Assessment.

represented in Figure 1. Baseline demographics and disease characteristics were mostly balanced between the IXE and ADA groups (Table 1). Totals of 51.0% and 54.9% of IXE- and ADA-treated patients, respectively, had concomitant methotrexate (MTX) use at baseline, which was permitted throughout the study.

Efficacy on Skin, Nails, and Joints

In the subgroup of patients with active PsA and moderate-to-severe PsO at baseline, a significantly higher proportion of patients treated with IXE versus ADA simultaneously achieved the primary endpoint, ACR50 and PASI100, at W24 (40.8% versus 17.6%, P = 0.015) and W52 (38.8% versus 17.6%, P = 0.026); statistically significant differences were observed as early as W8 (Figure 2).

Complete skin clearance (PASI100 response) was achieved by a significantly higher proportion in the IXE versus ADA group at W24 (59.2% versus 27.5%, P = 0.002) and W52 (59.2% versus 25.5%, P = 0.001); significant differences were observed as early as W4 (the first PASI assessment) and maintained throughout the study (Figure 3A). Likewise, PASI90 response was significantly greater in IXE- versus ADA-treated patients at all time points starting at W4, except at W32 (Figure 3B). IXE- versus ADA-treated patients had more rapid PASI75 responses with a significantly higher proportion achieving PASI75 from W4 to W16, and numerically, but not significantly (except for W40), more patients achieving PASI75 through W52 (Figure 3C).

With regard to joint outcomes, no significant differences were observed in ACR50 at W24 and in ACR20, ACR50, or ACR70 responses between IXE- and ADA-treated patients through W52 (Table 2).

Nail PsO was prevalent in patients with active PsA and moderate-to-severe PsO, affecting 75.5% (n = 37) and 80.4% (n = 41) of IXE- and ADA-treated patients, respectively, at baseline (fingernail NAPSI ≥ 1). Baseline demographics and disease characteristics of patients with nail PsO were balanced between the IXE and ADA groups (data not shown). Complete clearance of fingernail PsO occurred in 75.7% of IXE- versus 51.2% of ADA-treated patients at W24 (P = 0.035), and a numerically higher proportion of IXE- versus ADA-treated patients had a NAPSI = 0 response at all time points through W52 (Figure 4A). The mean change from baseline in fingernail NAPSI score indicated a more rapid decrease overall and a statistically larger difference for IXE- versus ADA-treated patients at W40, and numerically greater for all other time points through W52 (-21.9 versus -20.9, P = 0.583) (Figure 4B).

Patient-reported Outcomes

The baseline DLQI scores for the subgroup of patients with active PsA and moderate-to-severe PsO were 16.9 (standard deviation [SD] ± 7.3) and 16.7 (SD ± 6.4) for IXE- and ADA-treated patients, respectively, which was reflective of the high disease burden of this subgroup (Table 1). In the IXE versus ADA group, significantly more patients reported no or only minimal impact of skin disease on their QoL (DLQI 0,1) at W24 (59.2% versus 33.3%, P = 0.016) and numerically more at W52 (55.1% versus 37.3%, P = 0.108) (Figure 5A). IXE- versus ADA-treated patients had a more rapid mean reduction in DLQI score from baseline. The mean change in DLQI was consistently greater in the IXE- versus ADA-treated patients and was statistically greater at W4 through W16 (Figure 5B).

The mean change in Itch NRS score from baseline and complete resolution of itch (Itch NRS = 0) were numerically higher (except for the mean change in Itch NRS score from baseline at W52, which was numerically equal) but not significantly different in the IXE versus ADA group at all timepoints through W52 (Figure 5C and D).

Safety

The frequency of TEAEs was similar in patients receiving IXE versus ADA (59.2% versus 58.8%) (Table 3); all TEAEs

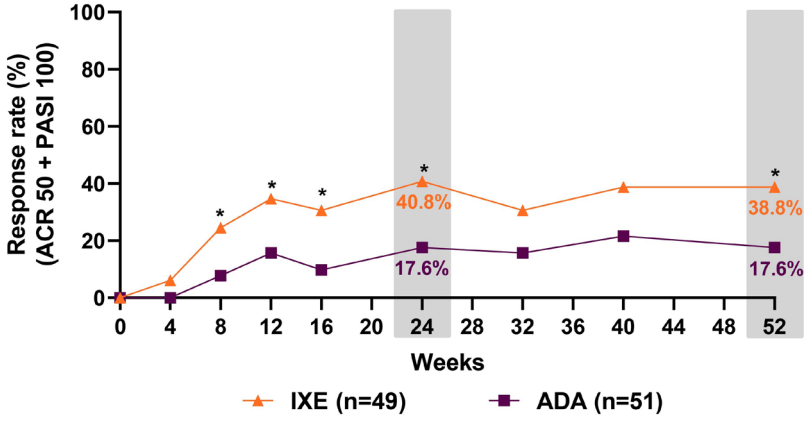

Figure 2. Percentage of patients with PsA and moderate-to-severe PsO simultaneously achieving ACR50 and PASI100 through Week 52. IXE versus ADA: * P ≤ 0.05.

ACR = American College of Rheumatology; ADA = Adalimumab; IXE = Ixekizumab; PASI = Psoriasis Area and Severity Index; PsA = Psoriatic arthritis; PsO = Plaque psoriasis.

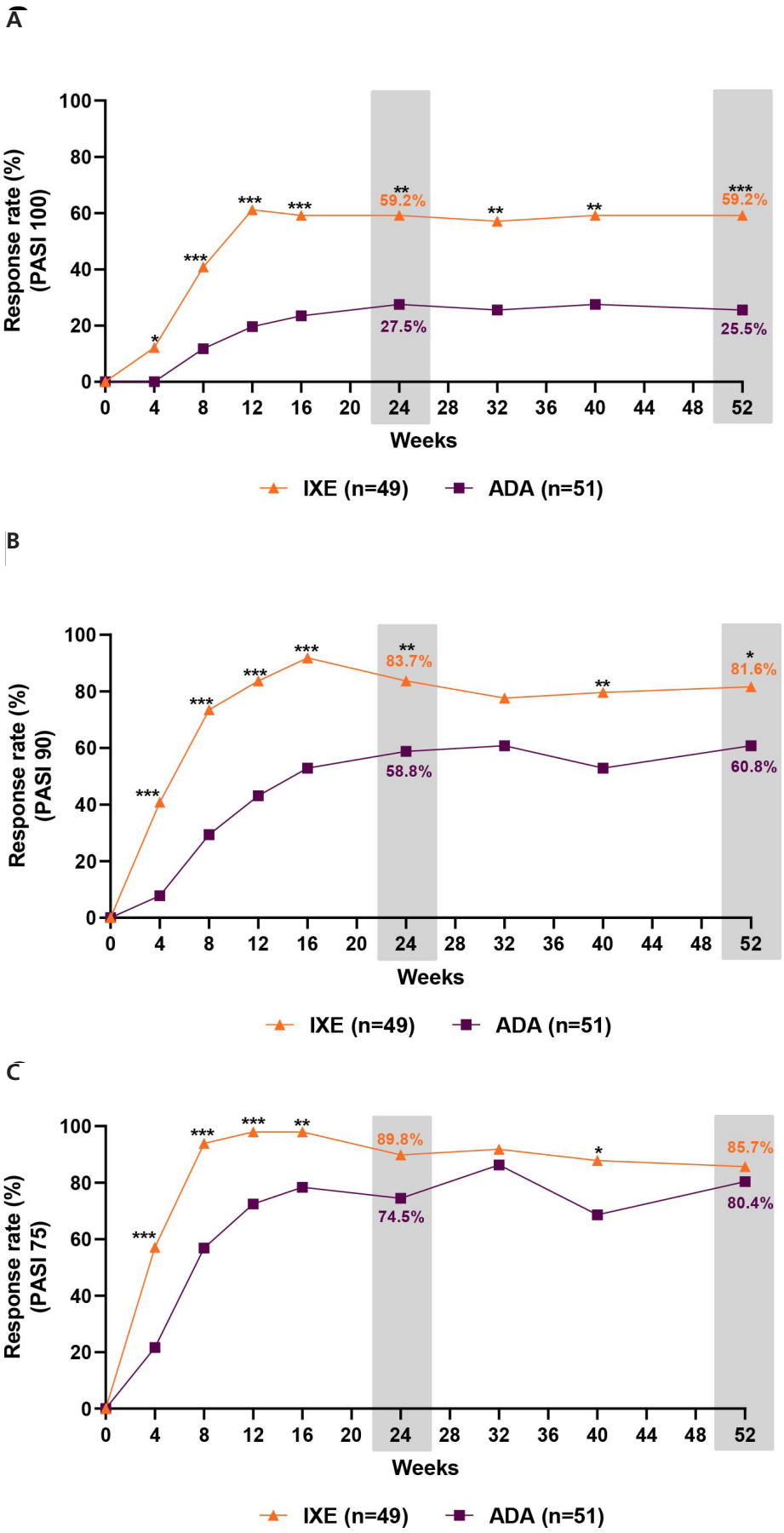

Figure 3. Skin outcomes through Week 52. Percentage of patients with PsA and moderate-to-severe PsO achieving (A) PASI100, (B) PASI90, and (C) PASI75. IXE versus ADA: * $P \leq 0.05$, ** $P \leq 0.01$, *** $P \leq 0.001$.

ADA = Adalimumab; IXE = Ixekizumab; PASI = Psoriasis Area and Severity Index; PsA = Psoriatic arthritis; PsO = Plaque psoriasis.

Table 2. Joint outcomes at Weeks 24 and 52

	Week 24				Week 52			
	IXE (n = 49)	ADA (n = 51)	Treatment difference IXE versus ADA (95% CI)	P[a]	IXE (n = 49)	ADA (n = 51)	Treatment difference IXE versus ADA (95% CI)	P[a]
ACR70	21 (42.9)	17 (33.3)	9.5 (-9.4, 28.5)	0.411	21 (42.9)	20 (39.2)	3.6 (-15.6, 22.9)	0.839
ACR50	29 (59.2)	28 (54.9)	4.3 (-15.1, 23.7)	0.691	27 (55.1)	32 (62.7)	-7.6 (-26.9, 11.6)	0.542
ACR20	37 (75.5)	40 (78.4)	-2.9 (-19.4, 13.6)	0.814	36 (73.5)	41 (80.4)	-6.9 (-23.4, 9.6)	0.480

Unless otherwise indicated, values are presented as n (%).
[a]P value: IXE versus ADA
ACR = American College of Rheumatology; ADA = Adalimumab; CI = Confidence intervals; IXE = Ixekizumab.

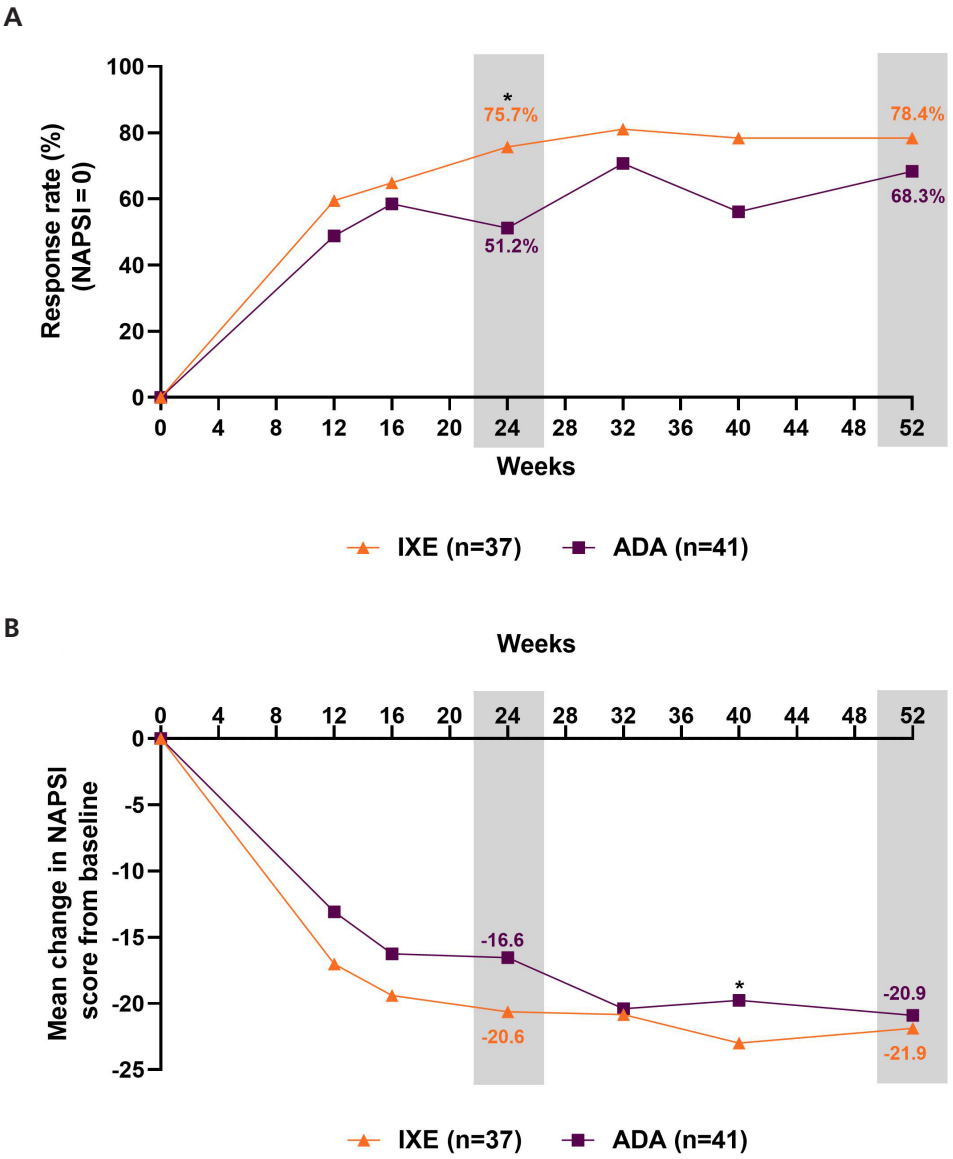

Figure 4. Clinical response rate for Fingernail PsO endpoints through Week 52. Graphs depict results for patients with moderate-to-severe PsO, PsA and a fingernail NAPSI ≥ 1 score at baseline. (A) Percentage of patients achieving fingernail NAPSI = 0 through Week 52. (B) Mean change in fingernail NAPSI score from baseline through Week 52. IXE versus ADA: * P ≤ 0.05, **P ≤ 0.01.

ADA = Adalimumab; IXE = Ixekizumab; NAPSI = Nail Psoriasis Severity Index; PsA = Psoriatic arthritis; PsO = Plaque psoriasis.

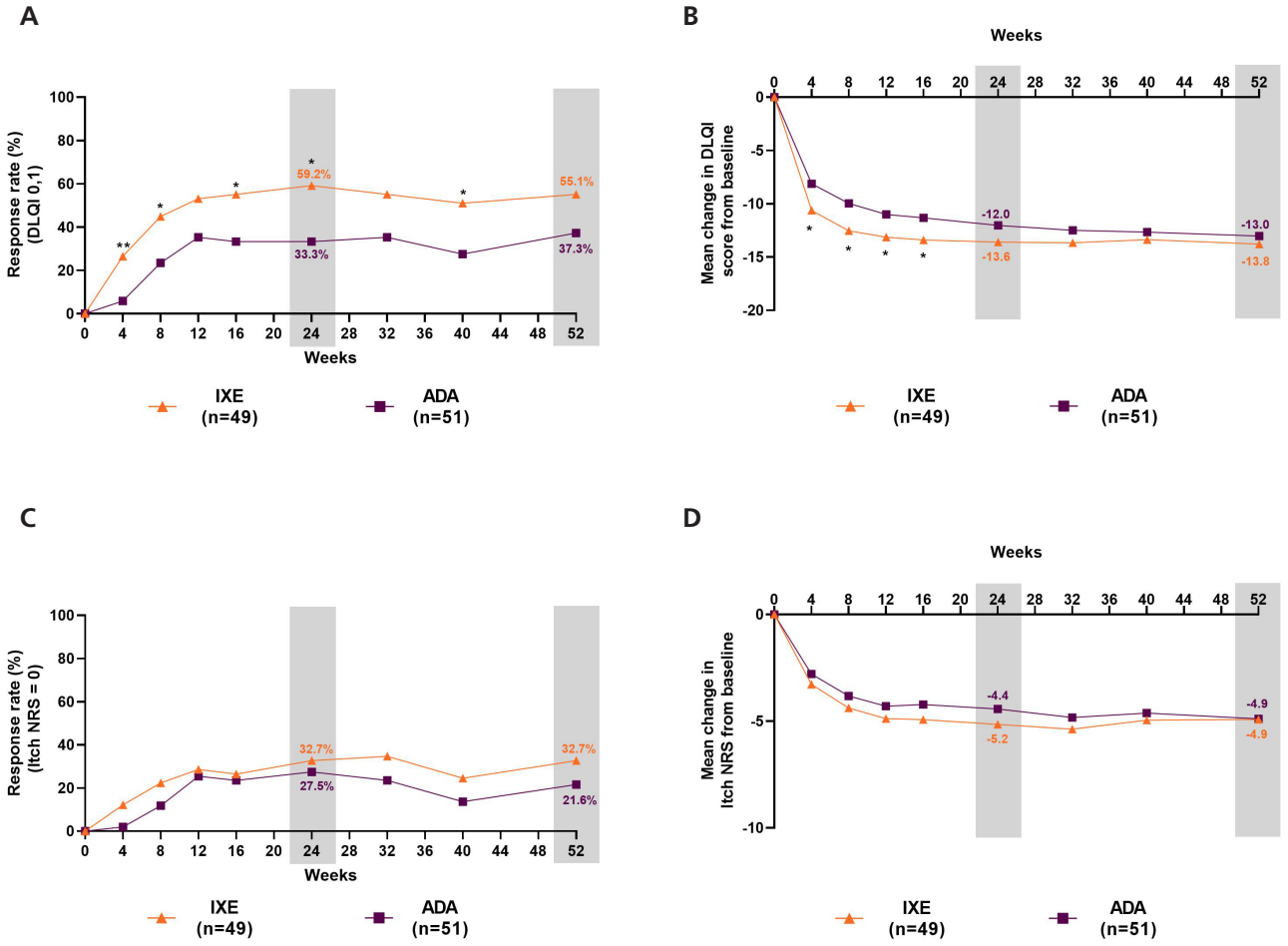

Figure 5. Clinical response rate for quality-of-life endpoints through Week 52. Graphs depict results for patients with PsA and moderate-to-severe PsO at baseline. (A) Percentage of patients achieving DLQI (0,1) through Week 52. (B) Mean change from baseline in DLQI score through Week 52. (C) Percentage of patients achieving Itch NRS = 0 through Week 52. (D) Mean change from baseline in Itch NRS score through Week 52. IXE versus ADA: * P ≤ 0.05, **P ≤ 0.01.

ADA = Adalimumab; DLQI = Dermatology Life Quality Index; IXE = Ixekizumab; NRS = Numeric Rating Scale; PsA = Psoriatic arthritis; PsO = Plaque psoriasis.

in the IXE group and 86.7% in the ADA group were mild or moderate, while 13.3% in the ADA group were severe. The TEAEs are consistent with the known safety profiles of both drugs. The frequency of serious AEs (SAEs) was lower in IXE- versus ADA-treated patients (0.0% versus 9.8%) and a lower proportion of patients in the IXE group discontinued due to an AE compared with ADA group (2.0% versus 7.8%). No deaths occurred during the study.

Conclusions

This subgroup analysis focused on the biologic-naïve patients with active PsA and moderate-to-severe PsO at baseline in the SPIRIT-H2H trial, which demonstrated higher efficacy of IXE versus ADA in patients with active PsA and PsO, and determined that IXE is also more efficacious than ADA for simultaneously achieving ACR50 and PASI100 at W24 and W52 in this subgroup [18,19]. Overall, IXE-treated patients demonstrated higher responses for resolution of skin and nail manifestations of PsO versus ADA-treated patients and comparable response rates regarding improvement in joint symptoms. Importantly, while anti-TNF biologics have previously been recommended as the first-line biologic to treat patients with PsA and PsO, these results indicate that IXE is as good as, if not better than, ADA in treating patients with active PsA and moderate-to-severe PsO [24].

Moderate-to-severe PsO can have considerable negative effects on patients QoL, and the burden of disease can be further compounded by the presence of nail PsO and comorbid PsA. The IXE group had significantly more patients achieving DLQI (0,1) at W24 and numerically more through W52 compared with the ADA group, indicating that rapid and sustained skin clearance had important and clinically meaningful effects on QoL for patients with active PsA and moderate-to-severe PsO.

Table 3. Safety outcomes

Category	IXE (N = 49)	ADA (N = 51)
TEAE	29 (59.2)	30 (58.8)
TEAE by severity		
Mild	17 (34.7)	15 (29.4)
Moderate	12 (24.5)	11 (21.6)
Severe	0	4 (7.8)
Death	0	0
SAE[a]	0	5 (9.8)
Treatment discontinuation due to AE	1 (2.0)	4 (7.8)
AE of special interest		
Infections	13 (26.5)	18 (35.3)
Serious infections[b]	0	1 (2.0)
Injection site reactions[c]	2 (4.1)	0
Allergic/hypersensitivity reactions[d]	2 (4.1)	2 (3.9)
Cerebrocardiovascular events[e]	0	1 (2.0)
Depression	1 (2.0)	0

Data are presented as n (%).
[a]SAEs were acute abdomen disorder (n = 1), pyrexia (n = 1), cellulitis (n = 1), polyneuropathy (n = 1), and peripheral artery occlusion and necrosis ischemic vascular disorder (n = 1).
[b]Serious infection was cellulitis.
[c]Defined by High Level Term (HLT).
[d]No confirmed anaphylaxis reported after medical review.
[e]Cerebro-cardiovascular events are defined using terms from the following subcategories: cardiovascular death, myocardial infarction, hospitalization for unstable angina, hospitalization for heart failure, hospitalization for serious arrhythmia, hospitalization for hypertension, resuscitated sudden death, cardiogenic shock due to myocardial infarction, coronary revascularization procedure, neurologic-stroke, and peripheral vascular events.
ADA = Adalimumab; AE = Adverse event; IXE = Ixekizumab; SAE = Serious adverse event; TEAE = Treatment-emergent adverse event.

Nail PsO can substantially compromise patients' daily activities by causing pain and impairing hand mobility and is a particularly difficult to treat manifestation of PsO [8]. Improvement and clearance of nail PsO is a long process, partially due to the slow growth rate of nails, and consequently, efficacy cannot be evaluated before 12 weeks of treatment [25]. In our subgroup analysis, the proportion of patients experiencing nail PsO was higher than in other moderate-to-severe PsO clinical trial populations as all patients had concomitant active PsA, which is associated with higher rates of nail PsO than PsO [26,27]. Notably, IXE treatment resulted in a more rapid increase overall in clearance of nail PsO than ADA, with significantly more IXE- versus ADA-treated patients demonstrating complete clearance of nail PsO at W24.

Previously published results from the IXORA-S trial have demonstrated that IXE is superior to ustekinumab, an anti-IL-12/23 biologic, in clearance of nail PsO at W24 [26]. Similarly, in the IXORA-R head-to-head trial comparing IXE with guselkumab (GUS), an anti-IL-23p19 biologic, IXE was superior to GUS in clearance of nail PsO at W24 [28]. The VOYAGE-1 and -2 trials demonstrated superiority of GUS to ADA in achieving clear/almost clear skin at W16; however, post hoc analysis demonstrated that improvements in nail PsO from baseline were higher for ADA versus GUS at W16, which suggests that the different methods of action of biologics may result in differing effects on specific PsO disease domains, such as nail PsO [29–31]. Importantly, our analysis of the SPIRIT-H2H subgroup with active PsA and moderate-to-severe PsO demonstrates that IXE has higher efficacy than ADA in achieving complete clearance of the skin and nails at W24. Overall, these and previously published results demonstrate the consistent high efficacy of IXE in achieving clearance of nail PsO. This is supported by multiple recent network meta-analyses, which report that IXE had the highest ranking among approved biologics (and small molecules in one network meta-analysis) for the treatment and/or clearance of nail PsO [32–34].

Of note, > 50% of patients in our subgroup analysis had concomitant MTX use at baseline. Previously published studies have indicated that concomitant MTX treatment improves the efficacy of ADA and other anti-TNF biologics in treating rheumatoid arthritis, but the results regarding the effect of this combined therapy for PsA have been inconclusive [35–38]. It has been suggested that in the overall SPIRIT-H2H study population, concomitant treatment with MTX increases the proportion of ADA-treated patients achieving simultaneous ACR50 and PASI100, or NAPSI =

0 at W52 but does not have a response-modifying effect in IXE-treated patients [39]. Therefore, it is possible that the proportion of ADA-treated patients achieving simultaneous ACR50 and PASI100, or clearance of nail PsO in our subgroup analysis is higher than would be observed in patients receiving ADA monotherapy.

The safety profiles of both IXE and ADA were consistent with previous clinical trials and the prescriber information for both drugs. The ADA group had numerically more SAEs (there were no SAEs in the IXE group) and treatment discontinuations due to AEs, which is consistent with previously published safety data from the overall SPIRIT-H2H trial [18,19].

The limitations of this study include the open-label design, which may have biased the outcome assessments. Another limitation is that while the data show clinically meaningful differences, the sample size was small and this post hoc analysis was not powered to demonstrate statistical differences between these subgroups.

In conclusion, this subgroup analysis demonstrated that IXE- versus ADA-treated patients achieved significantly greater simultaneous PASI100 and ACR50 responses through W52 and confirmed IXE as an efficacious and safe treatment for patients with active PsA and moderate-to-severe PsO. Additionally, comparison of the results of this analysis with those of other studies confirms the efficacy of IXE in treating nail PsO in patients with moderate-to-severe PsO, irrespective of concomitant active PsA [26-28]. These results increase awareness of available treatment options and inform evidence-based clinical decisions for patients with active PsA and moderate-to-severe PsO.

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